REMARKS

I. Specification

An amended Abstract of the Disclosure is being filed herein to replace the Abstract currently on file. In this regard, the Examiner's kind attention is directed to the fact that the expression "said hydrophobic block comprises 1.1 to 30 functional groups selected from the group consisting of carboxyl, amine, hydroxyl, amide, thiol and sulfonic acid groups, in a hydrophobic block chain of the copolymer" has been deleted and replaced with the following sentence: "The block copolymer comprises functional groups selected from the group consisting of carboxyl, amine, hydroxyl, amide, thiol and sulfonic acid groups, in the hydrophobic block chain of the copolymer, and the average number of the functional groups range from 1.1 to 30".

The number of functional group can be a rational number, because the functional groups are randomly introduced to the polymer chain during the polymerization process, and the number of functional group (z) per polymer chain represent the average number of repeating units of the inventive polymer (see, page 4, lines 25-26), which can be determined from the intensity of each peak of NMR (nuclear magnetic resonance) (see, page 7, lines 11-13). It is well known to a person of ordinary skill in the art that the number of functional group per polymer chain may be represented as a rational number.

Accordingly, Applicants respectfully request reconsideration and withdrawal of this objection.

II. Claim Objection

The objection of claim 12 under 37 CFR 1.03(c) as being in improper form because a multiple dependent claim cannot depend upon another multiple dependent claim, is respectfully traversed.

Claim 4 has been amended herein to depend from claim 1. None of claims 1-11 constitute a multiple dependent claim.

Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

III. Claim Rejections Under 35 U.S.C. § 112

The rejection of claims 1-8 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention, is respectfully traversed.

Applicants have amended claim 1 so that it is no longer open to ambiguity regarding the number of functional groups being claimed. The number of functional groups as claimed are represented by an average in a given number range. Moreover, as explained earlier, the number of functional groups per polymer chain need only be represented by a rational number.

Accordingly, the rejection of claims 1-8 under 35 USC 112, second paragraph, should be withdrawn.

IV. Claim Rejections Under 35 U.S.C. § 102

The rejection of claims 1-7 and 12-14 under 35 U.S.C. § 102(b) as being anticipated by Cha et al. USP 5,702,717 (hereinafter, referred to as "D1"), is respectfully traversed for the following reasons:

i) Critical feature of the present invention

The present invention as more clearly defined in claim 1, as amended, and claims 2-7, is directed to a micelle composition for a drug delivery system comprising an amphiphilic block copolymer having at least one hydrophilic blocks(A) and at least one hydrophobic blocks(B), wherein the block copolymer carries functional groups selected from the group consisting of carboxyl, amine, hydroxyl, amide, thiol and sulfonic acid groups, in the hydrophobic block chain of the copolymer, and the average number of the functional groups range from 1.1 to 30. The present invention is also directed to a pharmaceutical composition as claimed in claims 12-14 comprising a hydrophobic drug introduced in the hydrophobic block of the micelle composition of any of claims 1-11.

ii) Summary of Cited Reference D1

By way of review, the cited reference D1 teaches a system and method for parenteral delivery of hydrophilic drugs, in particular, highly water-soluble

peptide and protein drugs (see, col. 6, lines 31-34) encased in a biodegradable block copolymer in a liquid composition, wherein the biodegradable block copolymer comprises a hydrophobic A polymer block comprising a member selected from the group consisting of poly(*α*-hydroxy acids) and poly(ethylene carbonates), and a hydrophilic B polymer block comprising a polyethylene glycol.

iii) Comparison of the present invention with the teaching in D1

The drug delivery system as taught in reference D1 is designed specifically to administer a hydrophilic drug, particularly a highly water-soluble peptide and protein drug. On the other hand, the drug delivery system of the present invention is directed to administer hydrophobic drugs which are incorporated in the hydrophobic core of a micelle composition for the drug delivery system having an enhanced drug-loading capacity and sustained-release characteristics.

The micelle composition comprises an amphiphilic block copolymer having hydrophilic blocks and hydrophobic blocks with the block copolymer carrying functional groups selected from the group consisting of carboxyl, amine, hydroxyl, amide, thiol and sulfonic acid groups in the hydrophobic block chain of the copolymer, with the average number of functional group ranging from 1.1 to 30 to enhance the core's affinity to a hydrophobic drug. The term "functional group" in the present invention refers specifically to a hydrogenated functional group which effectively mediates interaction between a hydrophobic drug and the copolymer.

Further in the present invention, the hydrogenated functional group is introduced to the hydrophobic block chain of the copolymer by a) subjecting a functional monomer (e.g. 3-{(benzyloxycarbonyl)methyl}-1,4-dioxane-2,5-dione) to copolymerization with hydrophobic and hydrophilic blocks to obtain an amphiphilic block copolymer, wherein the hydrophobic block thereof comprises benzyl groups, and b) subjecting the copolymer to hydro-debenzylation under hydrogen in the presence of a catalyst (see page 5, lines 6-19).

The Examiner has pointed out that reference D1 teaches that the hydrophobic block can comprise malic acid and its functional group is a carboxylate. However, the carboxylate of malic acid is converted into an ester group under the reaction condition of reference D1 (see, col. 13, 'Scheme 1' and col. 15, 'Scheme 2').

Therefore, there exists no hydrogenated functional group in the hydrophobic block chain of the copolymer.

Accordingly, reference D1 clearly fails to teach a micelle composition for drug delivery comprising an amphiphilic block copolymer, wherein the block copolymer carries functional groups in an hydrogenated form having an average number in a range of 1.1 to 30 in the hydrophobic block chain of the copolymer to effectively mediate interaction between a hydrophobic drug and the copolymer, and fails to teach a pharmaceutical composition comprising a hydrophobic drug introduced in the hydrophobic block of the micelle composition.

Accordingly, claim 1 is clearly novel and the rejection under 35 USC 102(b) based upon reference D1, i.e., Cha et al., should be withdrawn.

V. Claim Rejections Under 35 U.S.C. § 103

The rejection of claims 1-14 under 35 USC 103(a) as being unpatentable over Cha et al. (reference D1), and the rejection of claims 1-7 and 12-14 under 35 U.S.C. § 103(a) as being unpatentable over Seo et al. (WO 01/87345; hereinafter, referred to as "D2"), is respectfully traversed for the following reasons.

As explained above in connection with the rejection under 35 USC 102, the reference D1 teaches a system and method for parenteral delivery of hydrophilic drugs, in particular, highly water-soluble peptide and protein drugs (see, col. 6, lines 31-34) encased in a biodegradable block copolymer in a liquid composition, wherein the biodegradable block copolymer comprises a hydrophobic A polymer block comprising a member selected from the group consisting of poly(*a*-hydroxy acids) and poly(ethylene carbonates), and a hydrophilic B polymer block comprising a polyethylene glycol.

In contrast, the present invention as set forth in independent claims 1 and 12, comprises an amphiphilic block copolymer having at least one hydrophophilic blocks and at least one hydrophobic blocks in which the block copolymer carries an average number of functional groups ranging from 1.1 to 30, in

an hydrogenated form in the hydrophobic block chain of the copolymer to effectively mediate interaction between a hydrophobic drug and the copolymer. Further, as discussed below, the inventive micelle composition and pharmaceutical composition show unexpected effects owing to the above feature of the block copolymer.

For all of the above reasons, the inventive micelle composition of claim 1 and the pharmaceutical composition of claim 12 and all claims depending on claims 1 and 12 are clearly patentable over reference D1. Accordingly, the rejection based upon 35 USC 103(a) in view of the teaching in reference D1 should be withdrawn.

The cited reference D2 (Seo et al.) discloses a composition capable of forming a polymeric micelle in a body fluid or an aqueous medium, said composition comprising an amphiphilic block copolymer having a hydrophilic A block component and a hydrophobic biodegradable B block component, wherein the biodegradable B block component of the copolymer is modified with an end group having affinity to a hydrophobic drug.

The Examiner has pointed out that reference D2 discloses several hydrophobic polymers that have functional groups that remain after the monomers were polymerized, but only one functional group of D2, which interacts with a hydrophobic drug, remains at the end terminal groups of the block copolymer (see, page 7, lines 24-27). Further, the functional group is capped by acylation with a

group such as a benzoyl group and acetyl group, thereby forming an ester capping (see, page 7, lines 9-14; page 9, lines 12-14). Therefore, there is no functional group of hydrogenated form in the hydrophobic block chain of the copolymer.

In contrast, the micelle composition in the drug delivery system of the present invention comprises an amphiphilic block copolymer, wherein the block copolymer carries an average number of functional groups in a range between 1.1 to 30, which are in non-capped, hydrogenated forms in the hydrophobic block chain of the copolymer to effectively mediate interaction between a hydrophobic drug and the copolymer.

For all of the above reasons, the cited reference D2 clearly fails to suggest or render obvious the micelle composition of the subject invention under 35 USC 103 and does not teach or suggest a pharmaceutical composition comprising a hydrophobic drug introduced in the hydrophobic block of the micelle composition of claim 1. Accordingly, the subject invention is clearly patentable over Seo et al. under 35 USC 103.

The present invention also exhibits unexpected beneficial effects. Owing to the functional groups having hydrogenated forms and being contained in the hydrophobic block, the pharmaceutical composition of the present invention comprising a hydrophobic drug introduced in the hydrophobic block of a micelle composition as claimed, has a markedly enhanced drug content and a prolonged

drug release time. Moreover, the micelle has a markedly reduced degradation time as compared with a pharmaceutical composition as taught in either of references D1 or D2, which teach a micelle composition having functional groups which are not contained in the hydrophobic block of the copolymer.

Specifically, as can be seen in the following Table, the content of which are identical to those disclosed in Tables 1 and 2 in the specification of the present application, a higher amount of the drug is contained in the hydrophobic core of the present invention compared to reference D1 or reference D2 represented by Comparative Example 1, which does not include functional groups in the hydrophobic block. The Examples 1-5 show a longer drug release time and a shorter degradation time for the micelle as compared to references D1 or D2 as represented by Comparative Example 1.

		Number of functional groups of the copolymer	Saturation drug content (wt%)	Drug release time (hr)	Degradation time of the micelle (day)
Present invention	Example 1	1.34	8.0	21	10
	Example 2	2.78	13.7	40	7
	Example 3	3.74	14.9	52	6
	Example 4	11.5	16.9	59	5
	Example 5	23.0	16.8	60	4
Comparative Example 1		**0**	**3.8**	**8**	**20**

As shown in the Table, as more functional groups are introduced into the hydrophobic block, the drug release time becomes longer. Therefore, by controlling the amount of carboxyl group introduced, a person skilled in the art can adjust the sustained-release characteristics of the composition. Further, with increasing the number of carboxyl groups introduced into the hydrophobic block, the micelle degradation time becomes shorter. Accordingly, a micelle composition having more functional groups will rapidly degrade after releasing the drug.

Accordingly, a micelle composition, in accordance with the present invention, comprising an average number of functional groups ranging between 1.1 to 30 in the hydrophobic block of the amphiphilic copolymer can carry a large amount of an hydrophobic drug, and exhibit sustained-release characteristics.

CONCLUSION

In view of the foregoing, it is respectfully submitted that the instant invention as defined in the pending claims 1-15 is not anticipated by nor obvious over the references cited by the Examiner, taken alone or in combination, and therefore, it is earnestly requested that the Examiner's rejections be withdrawn.

Reconsideration and allowance of claims 1-15 is respectfully solicited.

Respectfully submitted
Attorney for Applicant,

Dated: March 7, 2007

By: _____
Eugene Lieberstein
Registration No. 24,645

CUSTOMER NO.: 01109

ANDERSON KILL & OLICK, P.C.
1251 Avenue of the Americas
New York, New York 10020-1182
(212) 278-1000

CERTIFICATE OF MAILING

I hereby certify that this Amendment is being submitted to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 via EFS-Web on March 8, 2007.

_____
Audrey de Souza